**Susceptibility of Nosocomial Staphylococcus aureus to Chlorhexidine after Implementation of a Hospital-wide Antiseptic Bathing Regimen**

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### Abstract

Background: Bathing hospitalized patients with chlorhexidine gluconate is an effective way to reduce healthcare-associated infections by multi-drug-resistant organisms such as MRSA. There is concern that widespread use of chlorhexidine (CHX) will promote the emergence of bacterial resistance. This study assessed CHX susceptibility of bloodstream-infecting S. aureus from four distinct time periods with well-characterized usage of CHX patient bathing.

Methods: 104 freeze-banked S. aureus bloodstream isolates, recovered from patients hospitalized for greater than 72 hours, were selected for analysis. Four time periods were studied: (A) pre-CHX patient bathing (before 2009); (B) widespread use of CHX bathing during an institutional-wide study (Feb 2009-Aug 2010); (C) washout period with no use of CHX bathing (Sep 2010-Nov 2011); and (D) reintroduction of institutional-wide CHX patient bathing (Oct 2011-May 2015). CHX susceptibility was determined by broth microdilution. The Kruskal-Wallis test was used to compare the distribution of MIC between periods; the Mann-Whitney test with Bonferroni adjustment was used for pairwise comparisons between time periods. Isolates were also screened via PCR for the presence of qacA/B efflux pump encoding genes known to reduce susceptibility to CHX in S. aureus.

Results: Table 1 shows the number and percentage of isolates by MIC breakpoint. The mean MIC was significantly higher prior to widespread institutional use of CHX bathing compared to the other time periods (p=0.0081): mean MIC was significantly higher prior to widespread institutional use of CHX bathing (Period A) compared to the other time periods (p=0.0081): mean MIC was significantly higher prior to widespread institutional use of CHX bathing (Period A) compared to the other time periods (p=0.0081). Furthermore, no isolates were found to harbor qacA/B resistance genes.

Conclusion: Use of an institution-wide CHX patient bathing program for several years has not been associated with decreased susceptibility of Staphylococcus aureus to the antiseptic. These findings support continued use of CHX as a safe and efficacious means of reducing nosocomial infections.

### Introduction

Hospital-acquired infections impact as many as 4% of all patients admitted to acute care facilities. Daily bathing using a solution containing chlorhexidine (CHX), commonly formulated as chlorhexidine gluconate, has shown benefits in reducing the incidence of nosocomial infections:

- Reduced acquisition of multi-drug resistant bacteria such as MRSA and VRE
- Prevention of central line-associated bloodstream infections (CLABSI) and decreased bacteremia
- Potential reduction of hospital-acquired Candida difficile-associated diarrhea

Unfortunately, CHX use may promote the emergence of resistance:

- In Taiwan, MRSA isolates with elevated CHX MIC (>4 μg/ml) increased from 1.7% to 46.7% from 1990 to 2005.
- Patients receiving daily bathing with CHX are more likely to have infecting organisms (MRSA and others) with reduced chlorhexidine susceptibility versus those not receiving such bathing.

qacA/B are plasmid borne genes that encode for efflux pumps that extrude CHX and other antibiotics. In staphylococci, the presence of qacA/B has been associated with reduced CHX susceptibility and nosocomial disease outbreaks. ²

In Asia, as many as 44% of MRSA isolates have been found to harbor qacA/B, versus 0.9% of clinical MRSA samples submitted to a United States surveillance network.

### Methods

Purpose of Study: To determine if widespread use of CHX was associated with decreased susceptibility of S. aureus to CHX. Bloodstream-infecting bacteria were selected from periods prior to CHX bathing (Period A), during study use (Period B), during post-study non-use/washout (Period C), and after CHX bathing protocol adoption/use (Period D).

The null hypotheses were that neither overall susceptibility to chlorhexidine, nor qacA/B gene prevalence, would change during or after trial and adoption of chlorhexidine bathing.

**Hospital-acquired S. aureus bacteremia was defined by symptom onset and positive blood sample occurring more than 72 hours after admission, to exclude community-acquired infections.** ¹,¹⁰ Banked blood samples, frozen at –70°C, were used from Nebraska Medical Center inpatients with Staphylococcus bacteremia.

<table>
<thead>
<tr>
<th>Period</th>
<th>Sampling Dates</th>
<th># Accepted</th>
<th># Recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (Group A)</td>
<td>12/2007 - 12/2008</td>
<td>39</td>
<td>32</td>
</tr>
<tr>
<td>Widespread CHX use (Group B)</td>
<td>02/2010 - 06/2010</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Washout (Group C)</td>
<td>02/2011 - 09/2011</td>
<td>24</td>
<td>16</td>
</tr>
<tr>
<td>Widespread CHX use (Group D)</td>
<td>07/2014 - 05/2015</td>
<td>39</td>
<td>37</td>
</tr>
</tbody>
</table>

### Results

**Bloodstream-infecting S. aureus strains have not developed increased resistance to CHX over a 6 year time span including 2 distinct periods with widespread use of CHX. Indeed, a decline in average MIC was seen, and was significant when comparing control (period A) to washout (C) and implementation (D) periods.**

No qacA or qacB possessing organisms were discovered in the 22 screened strains with the highest CHX MIC.

### Conclusion & Future Direction

Bloodstream-infecting S. aureus strains have not developed increased resistance to CHX (over a 6 year time span including 2 distinct periods with widespread use of CHX). Indeed, a decline in average MIC was seen, and was significant when comparing control (period A) to washout (C) and implementation (D) periods. No qacA or qacB possessing organisms were discovered in the 22 screened strains with the highest CHX MIC.

- **Limitations:**
  - Sample size
  - MSSA vs. MRSA inclusion
  - qacA/B prevalence variation
  - Susceptibility testing

This study reassures that widespread institutional use of CHX for patient bathing over a period of several years has not been associated with the emergence of S. aureus with reduced susceptibility to CHX, and supports CHX patient bathing as a method to reduce healthcare-associated infections and transmission of multi-drug resistant organisms.

However, continued monitoring of chlorhexidine MICs is warranted to detect emergence of CHX resistance.

### References